# Coexistence of Mandibular Arteriovenous Malformation and Cerebellar Arteriovenous Malformation

## An Example of Cerebrofacial Arteriovenous Metameric Syndrome Type III

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***Summary***

*We describe a patient with cerebellar and mandibular arteriovenous malformations who initially presented with oral haemorrhage and then subsequently had a cerebellar haemorrhage. This is the second reported case of cerebrofacial arteriovenous metameric syndrome type III (CAMS III) in the literature and we discuss the role of homeobox genes in craniofacial development and angiogenesis.*

### Introduction

Cerebrofacial arteriovenous metameric syndromes (CAMS) are a recently published classification system for patients harboring both brain arteriovenous malformations (AVM) and facial-orbital AVMs [1]. These patients would formerly have been diagnosed with Wyburn-Mason or Bonnet-Dechaume-Blanc syndrome. They are thought to reflect metameric disorders of the neural crest or adjacent cephalic mesoderm prior to migration. CAMS I has involvement of the hypothalamus and nose. CAMS II involves the occipital lobe, thalamus, and maxilla. The CAMS III subtype indicates involvement of the cerebellum, pons, and mandible. The present case is the second report in the world literature of CAMS III.

### Case Report

A previously healthy girl presented at age six when an erupted left mandibular molar leading to profuse haemorrhage which stopped spontaneously. Thereafter, intermittent bleeding had occurred up to three times per day. Her parents had noticed vessel markings on the skin of her left lower face and neck since age two.

Initial angiography showed that the internal carotid artery injections were normal bilaterally. Vertebral artery injection was not performed. A large high flow facial AVM was present and supplied by left facial and deep masseteric branches, right facial and lingual arteries (figure 1). The nidus was inferior and lateral along the body of the left mandible. It drained into a large cavernous space which occupied the left hemimandible (figure 2) and then ultimately into a venous plexus which emptied into the left internal jugular vein.

At age seen, because of multiple episodes of bleeding from the left mandibular molar, the left lingual, facial, deep masseteric, transverse facial and right facial arteries were embolized with polyvinyl alcohol (PVA) particles and N-butyl cyanoacrylate (NBCA). NBCA was also directly injected into the left inferior dental vein. Two left mandibular molars were extracted. One month later, she was readmitted with

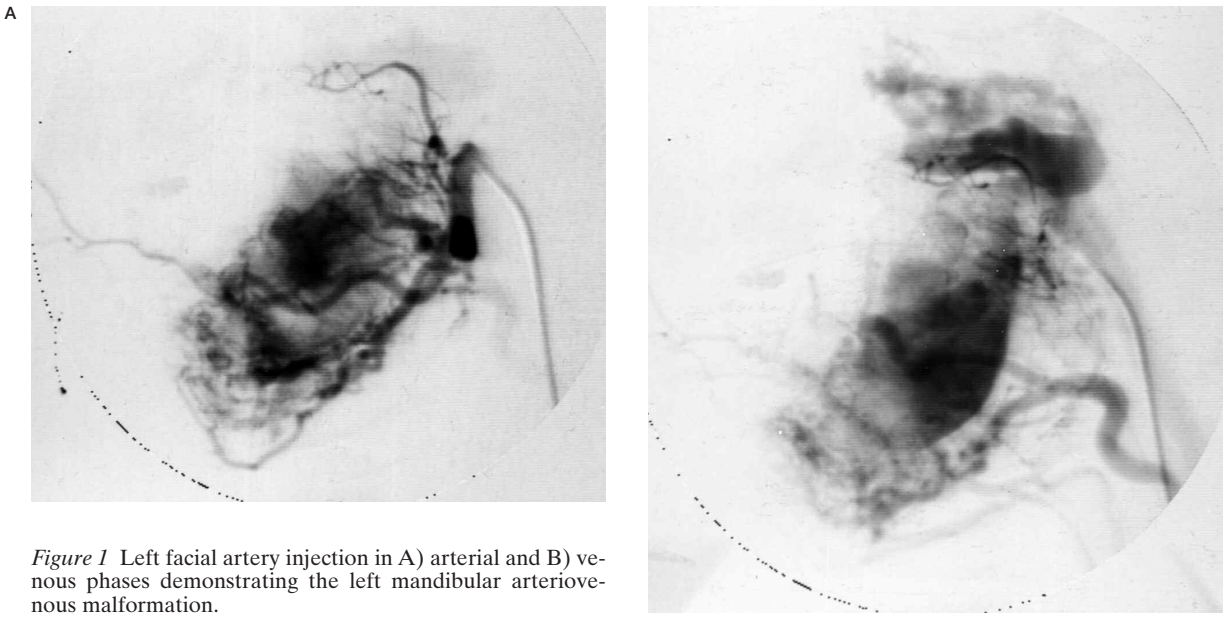


*Figure 1* Left facial artery injection in A) arterial and B) venous phases demonstrating the left mandibular arteriovenous malformation.

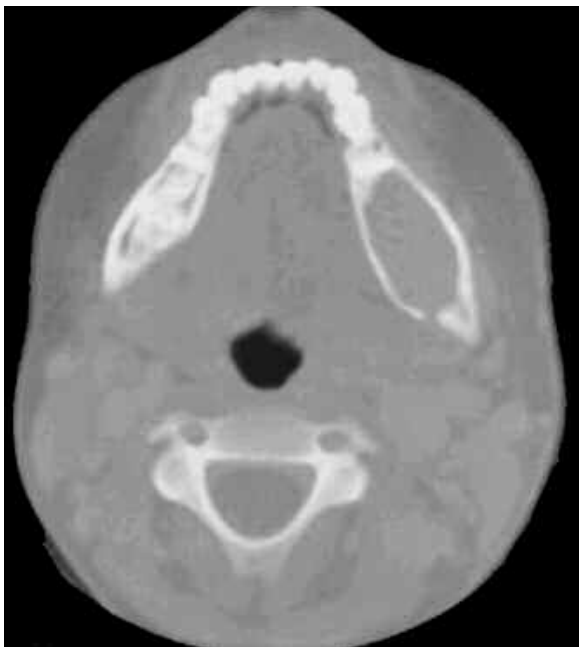

*Figure 2* Axial CT of the mandible showing the large cavernous space in the left mandible participating in the venous drainage of the facial AVM.

further haemorrhage. The right lingual, left transverse facial, internal maxillary, and facial arteries were reembolized. Four direct percutaneous injections of NBCA were made into the left hemimandible. Three months later, she developed swelling in the left preauricular area. Angiography showed recurrent AVM with profuse small collaterals from internal maxillary, transverse facial, facial, and external carotid arteries. Transverse facial, masseteric, distal external carotid, proximal internal maxillary and left facial arteries were embolized.

At age eight, biopsy of a left cheek mass showed recurrent AVM which was treated with left partial mandibulectomy and AVM resection. The mandibular defect was reconstructed with a vascularized free fibular graft.

At age twelve, the patient presented with headache, vomiting, and then collapse which progressed to respiratory arrest and neurogenic pulmonary oedema. Computed tomography showed a large left cerebellar haemorrhage which was treated with insertion of ventriculostomy and drainage of cerebellar haematoma. Postoperative angiogram (figure 3) showed a large left cerebellar AVM fed by an enlarged left anterior inferior cerebellar artery (AICA) and descending hemispheric branches of the left superior cerebellar artery (SCA). A separate AVM in the left ear pinna was fed by superficial temporal and posterior auricular arteries. No residual AVM was seen in the mandibular area. Embolization of the cerebellar AVM was attempted but unsuccessful.

Craniotomy and cerebellar AVM excision was performed. Postoperative angiogram showed residual AVM fed by left AICA and

SCA branches. Later that same year, the patient was treated with Gamma knife radiosurgery. Three year post-radiosurgery angiogram showed residual AVM with diffuse nidus supplied by left SCA, AICA, and posterior inferior cerebellar artery (PICA).

At the latest follow-up, the patient exhibited residual moderate truncal ataxia and mild left limb ataxia. Most recent angiography showed residual cerebellar AVM supplied by left SCA and AICA branches as well as a tiny AVM nidus in the midbrain and recurrent/residual left mandibular AVM supplied by bilateral facial and lingual arteries.

## Discussion

The only previous report of CAMS III was a 19 year old woman who presented with repeated bouts of haemorrhage from the area of her loose right mandibular molars. Ophthalmic examination showed a right optic nerve and retinal arteriovenous malformation. Cerebral angiography displayed an extensive AVM of her vermis, cerebellar hemispheres, and upper brainstem. In addition, a right facial AVM was present that drained into a large vein in the right mandibular ramus. No follow-up clinical information was provided [2].

Syndromes characterized by brain AVMs and facio-orbital AVMs have been recognized since the 1930's when they were first described by Bonnet, Dechaume, and Blanc, and then six years later, by Wyburn-Mason. The pathogenesis of Wyburn-Mason syndrome (otherwise known as Bonnet-Dechaume-Blanc syndrome) is still unclear. However, the uncommon occurrence of a brain AVM with a facial-orbital AVM suggests a metameric, or segmental, disorder of angiogenesis [1].

Homeobox (Hox) genes are a family of genes first described in Drosophila that are responsible for specifying the correct segment identity during embryonic development. They are important for hindbrain and craniofacial development [3]. Specifically, the human face arises from outgrowth and fusion of five facial processes: a frontonasal process, two maxillary processes, and two mandibular processes. The mandibular and maxillary processes develop from the first branchial arch. Branchial arch patterning is closely related to the hindbrain which is a segmented structure with transitory bulges called rhombomeres. The rhombomeres give rise to neural crest cells which migrate into specific branchial arches and facial processes where they form the facial bones and connective tissue. Conversely, facial muscles are derived from the paraxial mesoderm which forms

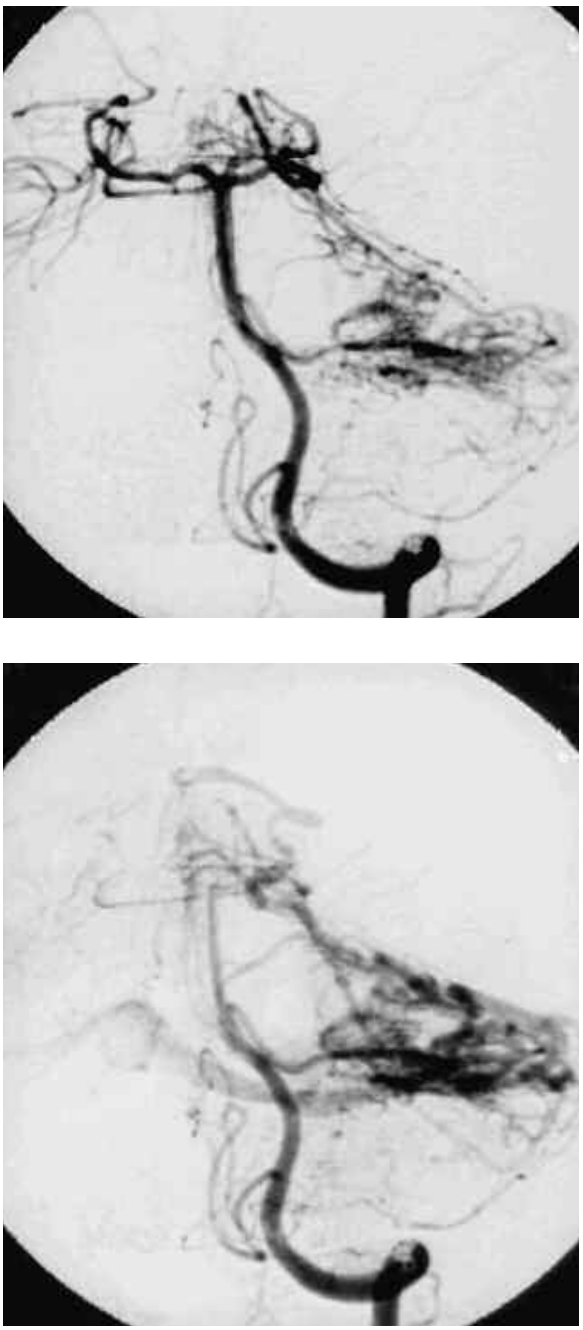


*Figure 3* Left vertebral artery injection in A) early arterial and B) late arterial phases showing the left cerebellar AVM with arterial supply from the left superior cerebellar and anterior inferior cerebellar arteries.

at the time of gastrulation and subsequently segments to form somitomeres in the head. Cells from somitomeres migrate into facial processes to form the facial muscles. Homeobox genes give positional identity to cells in the developing embryo by interpreting positional signals that exist in the embryo. Specific defects in homeobox genes have been associated with craniofacial abnormalities.

Homeobox genes are also important in angiogenesis. Endothelial cells express several members of the Homeobox gene family. The Hox D3 member of the homeobox gene family produces endothelial cell adhesion, invasion, and migration during angiogenesis which is required for the formation of new vascular sprouts. Constitutive expression of Hox D3 produces vascular malformations or endotheliomas which ultimately results in the formation of large haemorrhagic zones [4]. On the other hand, Hox B3 is required by sprouting endothelial cells for capillary morphogenesis [5]. As arteriovenous malformations are composed of a nidus where arteries are shunting into veins without interposed capillaries, the possibility of homeobox genes being involved in AVM development is tantalizing but at this time remains speculative.

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